

Pending claims w/ examiner's amdt. 9/30/2004 SBC

Appl. No. 10/006,882  
Amdt. dated September 2, 2004

PATENT

**Amendments to the Claims:**

This listing of claims will replace all prior versions, and listings of claims in the application:

**Listing of Claims:**

Claim 1 (currently amended): A method for continuous production of Hepatitis A virus (HAV) antigen, comprising the steps of providing a serum free cell culture of VERO cells bound to a microcarrier; growing the VERO cells in said serum free cell culture; infecting said serum free cell culture of VERO cells with HAV at a reduced temperature compared to the step of growing the cells; incubating said serum free cell culture of VERO cells infected with HAV to propagate said HAV at the reduced temperature, whereby HAV antigen is continuously released into the cell culture medium because infected cells release at least 50% of viral antigen into said medium; and harvesting said HAV antigen released into said medium.

Claim 2 (previously presented): The method according to claim 1, wherein said cells are grown at a temperature of about 37°C.

Claim 3 (previously presented): The method according to claim 2, wherein said reduced temperature is about 34°C prior to infection.

Claim 4 (previously presented): The method of claim 1, wherein the microcarrier is selected from the group consisting of spherical microcarriers and porous microcarriers.

Claim 5 (previously presented): The method according to claim 4, wherein the microcarriers comprise dextran, gelatine, collagen, plastic, or cellulose.

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Claim 7 (previously presented): The method according to claim 1, wherein the cells are infected with HAV at a multiplicity of infection between about 0.01 and about 5.0.

Claim 8 (previously presented): The method according to claim 1, wherein the cell culture is subcultured from a working cell bank and passaged by use of a microbial protease or a trypsin-like enzyme of a microbial origin.

Claim 9 (previously presented): The method according to claim 8, wherein said microbial protease is the purified trypsin-like enzyme of *Streptomyces griseus* Pronase.

Claim 10 (currently amended): The method according to claim 1, wherein the cells bound to the microcarrier continuously produce and release HAV antigen into the cell culture medium for at least 60 days.

Claim 11 (previously presented): The method according to claim 1, wherein said serum free cell culture of VERO cells is a serum and protein free cell culture of VERO cells.

Claims 12-23 (canceled).

Claim 12 (new). The method of claim 1, wherein the HAV antigen released into said medium is a complete HAV particle.

Claim 13 (new). The method of claim 12, further comprising isolating the complete HAV particle from the HAV harvest.

Claim 14 (new). The method of claim 13, wherein the complete HAV particle is isolated by isopycnic centrifugation.